

## ***Remarks***

### ***I. Status of the Claims***

Claims 81 and 82 are pending in the application, with claim 81 being the sole independent claim.

### ***II. Summary of the Office Action***

In the Office Action dated November 5, 2003, the Examiner has made one rejection of the claims. Applicants respectfully offer the following remarks to overcome or traverse this rejection.

### ***III. The Rejection Under 35 U.S.C. § 103(a) Over Goff In View of Arnold Is Traversed***

In the Office Action at section 4, pages 3-4, the Examiner has rejected claims 81 and 82 under 35 U.S.C. § 103(a) over Goff *et al.*, U.S. Patent No. 4,943,531 (Doc. "A" cited on the Form PTO-892 attached to Paper No. 17; hereinafter "Goff") in view of Arnold *et al.* (Doc. "U" cited on the Form PTO-892 attached to Paper No. 1003; hereinafter "Arnold"). Applicants respectfully traverse this rejection.

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the

invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). There is no basis for concluding that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time the invention was made. *See Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1995). Instead, the law requires a reason, suggestion, or motivation in the prior art that would motivate one of ordinary skill to combine the cited references, and that would also suggest a reasonable likelihood of success in making or using the claimed invention as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, the Examiner has not met this burden.

Claims 81 and 82 are drawn to methods of producing cDNA molecules from mRNA molecules using one or more reverse transcriptases in the presence of one or more double stranded inhibitory nucleic acids under conditions sufficient to synthesize cDNA molecules complementary to all or a portion of the mRNA template or under conditions sufficient to prevent nucleic acid synthesis. In contrast, Goff discloses plasmids encoding reverse transcriptases (and host cells comprising such plasmids), methods for producing such reverse transcriptases, and methods of using the reverse transcriptases to produce cDNA molecules. Importantly, however, Goff does *not* disclose the use of double stranded nucleic acid molecules as inhibitors of reverse transcriptase activity -- which the Examiner explicitly acknowledges (*see* Office Action at page 3, final sentence). Moreover, Goff does *not* disclose, suggest or otherwise contemplate the use of *any* inhibitors of reverse transcriptase activity in methods of producing cDNA molecules.

Therefore, Goff is seriously deficient as a primary reference upon which to base a *prima facie* case of obviousness.

These deficiencies of Goff are not cured by the disclosure of Arnold. The disclosure of Arnold is limited to a report of the crystal structure, at 7 Å resolution, of HIV-1 reverse transcriptase complexed with DNA. However, Arnold does *not* disclose the use of double stranded nucleic acid molecules as inhibitors of reverse transcriptase activity. Moreover, Arnold does *not* disclose, suggest or otherwise contemplate the use of *any* inhibitors of reverse transcriptase activity in methods of producing cDNA molecules. Hence, neither Goff nor Arnold discloses all of the elements of the presently claimed invention. Accordingly, a *prima facie* case of obviousness cannot be established based on the disclosures of these references.

In the attempt to overcome these deficiencies in the references themselves, the Examiner contends that one of ordinary skill in the art at the time the invention was made would have been motivated "to combine and substitute the method, wherein a double stranded nucleic acid is allowed to bind to the reverse transcriptase in order to inhibit the nucleic acid synthesis of Arnold *et al.* in the method of Goff *et al.*, since Arnold *et al.* state, 'These results have important implications for developing improved inhibitors of reverse transcriptase for the treatment of AIDS (Abstract, last sentence)'." Office Action at page 4. However, this cryptic statement in Arnold, and thus the Examiner's contention that is based on this statement, is irrelevant to the patentability of claims 81 and 82 for at least the following reasons.

First, the mere fact that references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990). As noted above, neither Goff nor Arnold discloses the production and use of double-stranded nucleic acids that function as reverse transcriptase inhibitors. Moreover, neither Goff nor Arnold suggests that double-stranded nucleic acid molecules should or even could be used in a method of producing cDNA molecules from mRNA molecules. Absent such suggestion and motivation, the cited references may not be properly combined to render the claimed invention obvious. *See In re Fine*, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Thus, the Examiner has not met the burden required to sustain a *prima facie* case of obviousness.

Second, even assuming *arguendo* that the disclosures of Goff and Arnold could be properly combined (which, as noted above, they cannot), this combination would not enable one of ordinary skill to make and use the claimed methods. As noted above, neither Goff nor Arnold discloses, suggests or contemplates making using double-stranded nucleic acids as reverse transcriptase inhibitors. As also noted above, neither Goff nor Arnold discloses, suggests or contemplates producing cDNA from mRNA using one or more reverse transcriptases in the presence of such double-stranded inhibitory nucleic acids. The cryptic statement in the abstract of Arnold, referred to by the Examiner, is nothing more than a general prompt that one should try and make an improved reverse transcriptase inhibitor. Hence, even if one of ordinary skill would have found proper motivation to have combined the disclosures of Goff and Arnold, this combination would not have resulted in the presently claimed invention.

Third, after reading the cryptic statement in Arnold discussed above, one of ordinary skill at best might have been motivated to try to make improved inhibitors of reverse transcriptase. However, whether a particular combination of elements might be obvious to try is not a legitimate test of patentability, and therefore cannot support a rejection under 35 U.S.C. 103. *See Amgen v. Chugai*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991); *In re O'Farrell*, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); *In re Fine*, 5 USPQ2d 1596, 1599 (Fed. Cir. 1988). Thus, the cryptic statement in Arnold relied upon in making the present rejection is irrelevant to the patentability of claims 81 and 82.

Finally, it appears that the Examiner is attempting to find the required motivation to combine the cited references in Applicants' own specification rather than in the cited art. However, as the Federal Circuit has held numerous times, such a hindsight analysis is impermissible. Instead, the Examiner must show suggestions, explicit or otherwise, that would compel one of ordinary skill to combine the cited references in order to make and use the claimed invention. *See, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143 (Fed. Cir. 1985) ("When prior art references require selective combination by the [fact-finder] to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself."); *Fine*, 5 USPQ2d at 1600 ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."); *In re Pleuddemann*, 910 F.2d 823, 828 (Fed. Cir. 1990) (noting that use of an applicant's specification as though it were prior art to support an obviousness determination is legal error); *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (holding that both the suggestion

to combine references, and a reasonable expectation of success in making the claimed invention, "must be founded in the prior art, not in the applicant's disclosure."). The Board has also provided the same mandate on this issue:

it is impermissible to use the claimed invention as an instruction manual or "template" to piece together isolated disclosures and teachings of the prior art so that the claimed invention may be rendered obvious . . . . a rejection based on § 103 must rest on a factual basis, with the facts being interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, the examiner has the initial duty of supplying the factual basis for the rejection he advances. He may not, because he doubts that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis.

*Ex parte Haymond*, 41 USPQ2d 1217, 1220 (Bd. Pat. App. Int. 1996). Thus, the hindsight analysis used in the present case is impermissible and cannot be used in the attempt to establish a *prima facie* case of obviousness.

For at least the above reasons, Applicants submit that upon careful analysis of the cited references, the skilled artisan would have found no motivation to combine the disclosures of the cited references so as to make and use the presently claimed invention. Accordingly, a *prima facie* case of obviousness has not been established.

In view of the foregoing remarks, reconsideration and withdrawal of the rejection of claims 81 and 82 under 35 U.S.C. § 103(a) over Goff in light of Arnold are respectfully requested.

***IV. Conclusion***

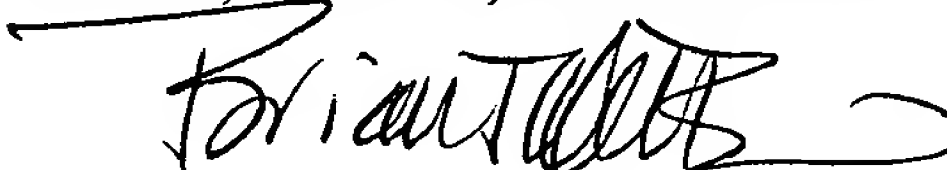
All of the stated grounds of rejection have been properly traversed. Applicants therefore respectfully request that the Examiner reconsider and withdraw the outstanding rejection.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt entry and favorable consideration of this Amendment and Reply, and allowance of all pending claims, are earnestly solicited.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in black ink, appearing to read "Brian J. Del Buono", with a stylized flourish at the end.

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